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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/049,893 | 07/22/2002 | David M Stern | 59472-A-PCT-US/JPW/FHB | 2372 |

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| EXAMINER | |
|---|---|
| EMCH, GREGORY S | |
| ART UNIT | PAPER NUMBER |
| 1649 | |

DATE MAILED: 01/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/049,893 | STERN ET AL. | |
| | Examiner | Art Unit | |
| | Gregory S. Emch | 1649 | |

*– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *42-70* is/are pending in the application.

4a) Of the above claim(s) *46-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-45 and 55-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/25/02 & 5/13/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Formal Matters*

Claims 57 and 58 were amended and new claim 70 was added in the communication dated 12 December 2005. Claims 42-70 are pending.

### *Election/Restrictions*

Applicant's election with traverse of Group I, claims 42-45 and 55-70, in the amendment dated 12 December 2005 is acknowledged. Applicant argues that there would not be a serious burden on the Examiner if restriction were not required, because a search of the prior art relevant to the claims of Group I would provide the relevant art for Groups II-VII. Since there is not burden on the Examiner to examine Groups II-VII together in the same application, the Examiner must examine the entire application on the merits.

Applicant's argument has been fully considered and is not found to be persuasive. Applicant's attention is directed to MPEP 808.02 which states that "Where the related inventions as claimed are shown to be distinct under the criteria of MPEP 806.05 (c-i), the examiner, in order to establish reasons for insisting upon restriction, must show by appropriate explanation one of the following: (A) Separate classification thereof; (B) A separate status in the art when they are classifiable together; (C) A different field of search."

In the instant case, Invention I requires administering sRAGE or a fragment thereof, which is not required by Inventions II-VII. Invention II requires administering an

antibody or portion thereof, which is not required by Inventions I and IV-VII. Inventions II and III are drawn to administration of different antibodies, which have independent and distinct properties, and a search of either of the inventions would not necessarily reveal art to the other Invention. Invention III requires administering an anti-RAGE antibody or portion thereof, which is not required by Inventions I and IV-VII. Invention IV requires administering a generic peptide, which is not required by Inventions I-III and V-VII. Invention V requires administering peptidomimetic, which is not required by Inventions I-IV, VI, and VII. Invention VI requires administering a nucleic acid, which is not required by Inventions I-V, and VII. Invention VII requires administering an organic compound with a molecular weight less than 500 daltons, which is not required by Inventions I-VI.

All seven Groups represent distinct and independent inventions the search and examination of which is not co-extensive and thus represents a search burden. Therefore, the lack of unity requirement set forth in the communication dated 11 September 2005 is still deemed proper and is therefore made FINAL. Hence, claims 42-45 and 55-70 are under consideration.

***Information Disclosure Statement***

Signed and initialed copies of the IDS papers filed 25 September 2002 and 13 May 2005 are enclosed in this action.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 42-45, 55-65, and 70 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 and 16 of copending Application No. 08/905,709 and claims 36, 39, 40 and 53 of copending Application No. 09/498,459.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably

distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

In the instant case, although the conflicting claims are not identical, they are not patentably distinct from each other because claim 1 of the '709 Application is drawn to a method of inhibiting atherosclerosis in a subject suffering from hyperlipidemia, which comprises administering to the subject a polypeptide comprising an extracellular domain of sRAGE capable of inhibiting an interaction between amyloid-$\beta$ peptide and RAGE in an amount effective to inhibit atherosclerosis in a subject. Further, claim 36 of the '459 Application is drawn to a method of inhibiting atherosclerotic plaque formation in a diabetic subject, which comprises administering to the subject a polypeptide comprising an extracellular domain of sRAGE capable of inhibiting an interaction between amyloid-$\beta$ peptide and RAGE.

The instantly claimed method is an obvious variation of the claims as set forth in the '709 and '459 Applications because as disclosed in the instant specification (p.36, lines 30-31) and in the instant claims 64 and 65, subjects of the instantly claimed method include those suffering from hyperlipidemia, as in the '709 Application, and those suffering from diabetes, as in the '459 Application. Also, "a compound capable of inhibiting binding of the $\beta$-sheet fibril to RAGE" is defined as sRAGE or a fragment thereof (p.26, line 31). Furthermore, the $\beta$-sheet fibril is defined by the instant

specification as comprising amyloid fibril, prion-derived fibril, or amyloid-$\beta$ peptide (p.26, lines 22-24). Claims 2 and 3 of the '709 Application and claims 39 and 40 of the '459 Application recite treating mammals and humans, as in the instant claims 59 and 60. Claim 16 of the '709 Application and claim 53 of the '459 Application recite the same limitations as the instant claim 61. Therefore, the claims of the copending Applications anticipate claims 42-45, 55-65, and 70 of the instant Application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 42-45, 55, 57-61, 63-68 and 70 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/26913 to Stern et al. (cited in Applicant's IDS from 13 May 2005).

The claims are to directed to a method for preventing and/or treating a disease involving $\beta$-sheet fibril formation, other than Alzheimer's Disease, in a subject which comprises administering to the subject a binding-inhibiting amount of a compound capable of inhibiting binding of the $\beta$-sheet fibril to RAGE so as to thereby prevent

and/or treat a disease involving β-sheet fibril formation other than Alzheimer's Disease in the subject.

The '913 document teaches a method for treating a subject with a condition associated with interaction of an amyloid-β peptide with a receptor for advanced glycation endproduct (RAGE), which comprises administering to the subject an agent capable of inhibiting the interaction between the amyloid β-peptide and RAGE, the agent being present in an amount effective to inhibit the interaction between the amyloid β-peptide and RAGE, thereby treating the subject (p.12, lines 19-27). The '913 document also teaches that the condition may be a number of disorders, e.g. diabetes, renal failure, hyperlipidemic atherosclerosis, ALS, neuronal cytotoxicity, MS, Down's syndrome, neuronal degeneration (p.12, lines 29-33). Also, the condition may be associated with amyloid β-peptide fibril or with aggregation of amyloid β-peptide (p.13, lines 5-6) and Aβ (1-40) is taught (p.20, line 10). Thus, the limitations of claims 42, 55, 57, 58, 63-68, and 70 are anticipated by the '913 document. Furthermore, the subject may be a mammal or human (p. 12, lines 33-34), and the administration may be intralesional, intraperitoneal, intramuscular, intravenous, liposome-mediated delivery, topical, nasal, oral, anal, ocular or otic delivery (p.12, line 34 – p.13, line 1), thus meeting the limitations of claims 59-61. Finally, the '913 document teaches that the agent may be sRAGE (p.10, lines 27-29), thus meeting the limitation of claims 43-35.

Since the document teaches all the elements of the claims, claims 42-45, 55, 57-61, 63-68 and 70 are anticipated by WO 97/26913 to Stern et al.

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 42-45, 55, 57-68, and 70 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,864,018 to Morser et al (cited in Applicant's IDS from 25 September 2002).

The claims are to directed to a method for preventing and/or treating a disease involving $\beta$-sheet fibril formation, other than Alzheimer's Disease, in a subject which comprises administering to the subject a binding-inhibiting amount of a compound capable of inhibiting binding of the $\beta$-sheet fibril to RAGE so as to thereby prevent and/or treat a disease involving $\beta$-sheet fibril formation other than Alzheimer's Disease in the subject.

The '018 patent discloses a method for inhibiting atherosclerotic plaque formation in a diabetic subject, which comprises administering to said subject a polypeptide which comprises a soluble extracellular portion of a receptor for advanced glycation endproduct (AGE) or a derivative thereof, said polypeptide being capable of inhibiting

an interaction between amyloid β-peptide and RAGE. The '018 patent also discloses compositions for blocking interaction between AGE and RAGE. Such compositions may be used to reduce the pathological effects of diabetes (col.4, lines 10-34, 54-64; col.19, lines 9-15). The interaction of AGEs with RAGE has been implicated in activation of microglial cells by amyloid β-peptide (col. 19, lines 15, 16). The composition may comprise soluble RAGE polypeptides or polypeptides related to and/or derived from RAGE. The soluble region lacks the transmembrane domain, and the polypeptides comprise fragments of the extracellular domain. The soluble peptides comprise one or more immunoglobulin-like domains. The polypeptides may inhibit AGE/RAGE interaction (col.5, lines 4-38; col.6, lines 1-16).

The β-sheet fibril is defined by the instant specification as comprising amyloid fibril, prion-derived fibril, or amyloid-β peptide (p.26, lines 22-24). Thus, a compound capable of blocking the interaction of amyloid-β peptide and RAGE would inherently be capable of blocking the interaction between a β-sheet fibril and RAGE. Thus, the limitations of claims 42, 55, 57 and 70 have been disclosed by the '018 patent.

Although the '018 patent did not appreciate Aβ (1-39), Aβ (1-40), Aβ (1-42) and Aβ (1-40) Dutch variant, claim 58 recites the open language "comprises," which allows for more than what is included in these species of amyloid-β peptide. Therefore, since the Morser et al. patent discloses amyloid-β peptide, said peptide would inherently include at least one of the species recited by claim 58.

The '018 patent also discloses sRAGE (col.5, lines 19-28), thus anticipating claims 43-45. The '018 patent discloses administration of the polypeptides to human

and non-human patients (col.18, lines 64-67; col.19, lines 1-31), thus meeting the limitations of claims 59 and 60. Further, the patent discloses that the a method of administration may be selected from oral, intravenous, intraperitoneal, intramuscular, or local administration (col.19, lines 57-67), thus meeting the limitations of claim 61. The '018 patent discloses prevention or treatment of disorders, such as Diabetes Mellitus, diabetic macrovasculopathy (atherosclerosis), neuropathy, nephropathy, occlusive vascular disorders, amyloidosis (col.19, lines 6-24), thus anticipating claims 62-68.

Since the patent discloses all the elements of the claims, claims 42-45, 55, 57-68, and 70 are anticipated by U.S. Patent No. 5,864,018 to Morser et al.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 42-45, and 55-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,864,018 to Morser et al., in view of Lilley et al. (Am Fam Physician 1998 Mar 1; 57(5): 1079-88), further in view of Kelley (Proc Natl Acad Sci U S A. 1998 Feb 3; 95(3): 930-2).

The claims are to directed to a method for preventing and/or treating a disease involving β-sheet fibril formation, other than Alzheimer's Disease, in a subject which comprises administering to the subject a binding-inhibiting amount of a compound capable of inhibiting binding of the β-sheet fibril to RAGE so as to thereby prevent and/or treat a disease involving β-sheet fibril formation other than Alzheimer's Disease in the subject.

The '018 patent discloses a method for inhibiting atherosclerotic plaque formation in a diabetic subject, which comprises administering to said subject a polypeptide which comprises a soluble extracellular portion of a receptor for advanced glycation endproduct (AGE) or a derivative thereof, said polypeptide being capable of inhibiting an interaction between amyloid β-peptide and RAGE. The '018 patent also discloses compositions for blocking interaction between AGE and RAGE. Such compositions may be used to reduce the pathological effects of diabetes (col.4, lines 10-34, 54-64; col.19, lines 9-15). The interaction of AGEs with RAGE has been implicated in activation of microglial cells by amyloid β-peptide (col. 19, lines 15, 16). The composition may comprise soluble RAGE polypeptides or polypeptides related to and/or derived from

RAGE. The soluble region lacks the transmembrane domain, and the polypeptides comprise fragments of the extracellular domain. The soluble peptides comprise one or more immunoglobulin-like domains. The polypeptides may inhibit AGE/RAGE interaction (col.5, lines 4-38; col.6, lines 1-16).

The β-sheet fibril is defined by the instant specification as comprising amyloid fibril, prion-derived fibril, or amyloid-β peptide (p.26, lines 22-24). Thus, a compound capable of blocking the interaction of amyloid-β peptide and RAGE would inherently be capable of blocking the interaction between a β-sheet fibril and RAGE. Thus, the limitations of claims 42, 55, 57 and 70 have been disclosed by the '018 patent.

Although the '018 patent did not appreciate Aβ (1-39), Aβ (1-40), Aβ (1-42) and Aβ (1-40), claim 58 recites the open language "comprises," which allows for more than what is included in these species of amyloid-β peptide. Therefore, since the Morser et al. patent discloses amyloid-β peptide, said peptide would inherently include at least one of the species recited by claim 58.

The '018 patent also discloses sRAGE (col.5, lines 19-28), as in claims 43-45. The '018 patent discloses administration of the polypeptides to human and non-human patients (col.18, lines 64-67; col.19, lines 1-31), as in claims 59 and 60. Further, the patent discloses that the a method of administration may be selected from oral, intravenous, intraperitoneal, intramuscular, or local administration (col.19, lines 57-67), as in claim 61. The '018 patent discloses prevention or treatment of disorders, such as Diabetes Mellitus, complications associated with diabetes, diabetic macrovasculopathy

(atherosclerosis), neuropathy, nephropathy, occlusive vascular disorders, and amyloidosis (col.19, lines 6-24), as in claims 62-68.

The '018 patent does not disclose treating a wound associated with diabetes. However, Kelley teaches that prion diseases result from $\beta$-sheets fibril formation (abstract), as in claim 56.

Neither the '018 patent nor Kelley teaches a prion-derived fibril. However, Lilley et al. teaches that diabetes mellitus is associated with delayed wound healing (abstract), as in claim 69.

Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to arrive at the claimed invention by combining the methods of treating atherosclerotic plaque formation in a diabetic subject disclosed by U.S. Patent No. 5,864,018 to Morser et al. with treating a prion disease as taught by Kelley and treating wounds associated with diabetes as taught by Lilley et al. The person of ordinary skill in the art would have been motivated to make these modifications in order to treat more of the complications associated with diabetes as taught by the '018 patent (col. 19, lines 6-24) and because compounds that prevent prion particle formation are important for therapeutics as taught by Kelley (p.932). The person of ordinary skill in the art would have had a reasonable expectation of success because the '018 patent teaches that it should work (entire document).

## *Conclusion*

No claims are allowed.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached on Monday through Friday from 8:30AM to 5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached at (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gregory S. Emch, Ph. D.
Patent Examiner
Art Unit 1649
January 26, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER